REMARKS

Claims 30-63 are pending in the instant application. Claims 30-63 have been rejected. Claim 30 has been amended. Support for this amendment is provided throughout the specification, for example at 17 and page 47. Claims 41, 50, 54 and 58 have been amended to depend from claim 30. No new matter is added by this amendment. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims 30-34 under 35 U.S.C. 102(b)

The rejection of claims 30-34 under 35 U.S.C. 102(b) as being anticipated by Malovrh et al. (Comparative Biochemistry and Physiology, Part C, 1999, p.221-226) has been maintained. The Examiner suggests that Malovrh et al. discloses a composition comprising a sponge toxin, sponge toxin comprising poly-APS, sponge toxin obtained from *Renieri sarai*, wherein the sponge toxin has a molecular weight between 5.0 kDa to 20 kDa. The Examiner suggests that Malovrh et al. is silent about the pore-forming property of the sponge toxin being reversible. However, the Examiner suggests that the prior art composition is the

same as the claimed composition and thus must necessarily exhibit the reversible pore-forming properties.

Applicants respectfully traverse this rejection.

Applicants respectfully disagree with the Examiner's characterization of Applicants' arguments submitted in the response filed July 3, 2008 as well as the Examiner's characterization of data in the application as compared to teachings of Malovrh et al.

In the second and third paragraphs of page 10 of the Office Action mailed October 17, 2008, the Examiner suggests that Applicants argued that Zn^{2+} prevents poly-APS pore formation when added after poly-APS. This is incorrect. The data in the application and Applicants' arguments indicate that Zn^{2+} prevents pore formation when added prior to or concurrent with poly-APS. The Examiner then goes on to assert that Malovrh *et al.* discloses the same properties, however, as Malovrh *et al.* only discloses the effects of Zn^{2+} when added after poly-APS, it cannot possibly disclose the same properties.

The Examiner further asserts in the final paragraph on page 10 of the Office Action that the present application does not discuss the effect of Zn^{2+} added after poly-APS on

the already formed pores. The Examiner references the quote "once poly-APS had produced pores.... zinc failed to...", which unambiguously discusses application of zinc after pores have been formed by poly-APS. Nevertheless, Applicants would like to bring to the Examiner's attention the data presented on page 32, lines 6 to 16, and Figure 6A of the instant specification which clearly shows that the addition of Zn^{2+} after poly-APS had been applied to a membrane and a pore had been formed, did not result in closure of that pore. Indeed, the addition of Zn^{2+} after a pore had been formed had no affect on the pore - note the line in Figure 6A does not noticeably change.

This is clearly the opposite to that taught in Malovrh *et al.* which explicitly states on page 225, second paragraph in column 1: "This fact and the ability of Zn^{2+} to inhibit already progressing lysis suggests that Zn^{2+} neither stabilizes nor prevents the binding of poly-APS to membrane. Rather, we suggest that **divalent cations close the resulted pores**" (emphasis added).

In the same paragraph of the Office Action, the Examiner appears to suggest that the data in the present application relating to the effect of Zn^{2+} and the data in

Malovrh *et al.* relating to Zn^{2+} cannot be compared because Malovrh *et al.* does not disclose experimental protocols with poly-APS and Zn^{2+} effects on membrane potential and conductivity. Applicants respectfully disagree. Indeed, the experiments in Malovrh *et al.* rely on absorbance to indicate the formation, or otherwise, of pores in cell membranes. However, measuring membrane potential, conductivity or absorbance are all merely tools with which to identify whether pores are present in the cell membrane. The tool used to identify pore presence or absence does not influence whether a pore is present or absent, and thus has no effect on the actual invention. The fact that Malovrh *et al.* uses absorbance and the present application uses membrane potential and conductivity is thus irrelevant. Further, as an aside, the present application does actually include experiments which rely on measuring absorbance, for example for determining changes in Ca^{2+} levels.

With regard to the first full paragraph on page 11 of the Office Action, the Examiner seems to interpret the phrase "reversible pore-forming sponge toxin" to mean that the pores in Malovrh *et al.*, which require Zn^{2+} to close, are formed by a "reversible pore-forming sponge toxin".

This phrase in claim 30 is intended to specify that the reversibility of the pore results from the toxin itself, rather than requiring any outside agent to close the pore.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 30 to recite a composition consisting essentially of a reversible pore-forming sponge toxin for the reversible formation of a membrane pore. This amendment is clearly supported by experiments set forth in the instant specification, for example at page 47, demonstrating that sponge toxin preparations alone were able to provide reversible pore formation without cytotoxicity.

Additional differences between the poly-APS of the present invention and that of Malovrh *et al.* include the fact that membrane recovery in the present invention occurred within approximately 20 minutes (see page 27, lines 24 to 26) whereas Figure 2 of Malovrh *et al.* clearly shows that at least 40 minutes after application of the lowest concentration of poly-APS (0.12 µg/ml), there was no recovery in membrane integrity. This further supports that the poly-APS in the present invention and the poly-APS Malovrh *et al.* do not have the same properties and thus

cannot be considered to be the same.

Furthermore, there is absolutely no reason, and indeed no evidence, why there cannot be more than one type of toxin derived from the marine sponge *R. sarai*. In view of the clear differences in activity between the sponge toxins in the present invention and those disclosed in Malovrh *et al.*, Applicants respectfully submit that these are different toxins and that the subject matter of the present invention is novel over Malovrh *et al.*

Withdrawal of the rejection under 35 U.S.C. 102(b) is therefore respectfully requested.

II. Rejection of Claims 30-40 and 60-63 under 35 U.S.C. 103(a)

The Examiner has also maintained the rejection of claims 30-40 and 60-63 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Malovrh et al. (Comparative Biochemistry and Physiology, Part C, 1999, p.221-226) and the rejection of claims 41-49 under 35 U.S.C. 103(a) as being unpatentable over Woude et al. (PNAS 1997 Vol. 94, p. 1160-1165) in view of Malovrh et al. (Comparative Biochemistry and Physiology, Part C, 1999,

p.221-226).

Applicants respectfully traverse these rejections.

At page 11 of the Office Action, the Examiner suggests that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and that this combination yielded nothing more than predictable results to one of ordinary skill in the art.

Applicants respectfully disagree.

Clear from Section I, supra, is that the sponge toxin of the instant application is different from that taught by Malovrh et al.

Further, Applicants have amended claim 30 to clarify that unlike the sponge toxin of Malovrh et al. which requires Zn^{2+} to reverse pore formation, a composition consisting essentially of a sponge toxin of the present invention reverses formation of membrane pores. Claims 41, 50, 54 and 58 have been amended to depend from claim 30.

Woude et al. discloses vesicle-mediated transfection into cells which is entirely different to the reversible pore-forming mechanism of action of the claimed sponge

toxins.

Accordingly, contrary to the Examiner's suggestion, all claimed elements were **not** known in the cited prior art.

Withdrawal of this rejection is respectfully requested.

III. Rejection of Claims 50-59 under 35 U.S.C. 103(a)

The Examiner has also maintained the rejection of claims 50-59 under 35 U.S.C. 103(a) as being unpatentable over Woude et al. (PNAS 1997 Vol. 94, p. 1160-1165) and Arendt et al. (Neuroscience, 1998, Vol. 85, No. 4, p. 1337-1340) in view of Ballard C.G. (European Neurology, 2002, Vol. 47, P. 64-70) and further in view of Bunc et al. (Toxicon 2002 Vol. 40, P. 843-849).

Applicants respectfully traverse this rejection.

At the outset, it is respectfully pointed out that claims 50 and 54 have been amended to depend from claim 30.

None of the cited references teach or suggest the composition of claim 30.

Instead, Woude et al. discloses vesicle-mediated transfection into cells which is entirely different to the pore-forming mechanism of action of the claimed sponge toxins.

Bunc et al. relates to the same poly-APS of Malovrh et al. (see col. 2, page 844 of Bunc et al.) and therefore, as demonstrated in Section I, supra, is different from the composition of claim 30.

References of Arendt et al. and Ballard are unrelated to in vivo transfection methods or sponge toxins.

Accordingly, the cited combination of references, none of which teach or suggest a composition as set forth in claim 30, cannot render obvious this independent claim.

MPEP 2143.03 and the case law are clear; if an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Accordingly, claims 50-59, which have been amended to depend from claim 30, must also be unobvious.

Withdrawal of this rejection under 35 U.S.C. 103(a) is therefore respectfully requested.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent

allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Kathleen A. Tyrrell
Registration No. 38,350

Date: **December 17, 2008**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515